JCI The Journal of Clinical Investigation

In This Issue

J Clin Invest. 2011;121(1):1-1. https://doi.org/10.1172/JCI46024.

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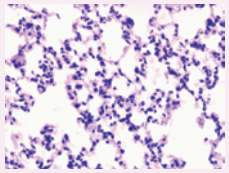
Intoxicating breast cancer cells with ROS



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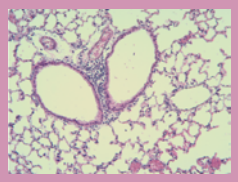
A benefit of flu: protection from asthma?

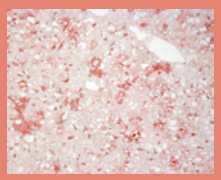


The number of people with asthma has increased sharply over the past few decades. It has been hypothesized that this is a result of decreased childhood exposure to microorganisms. Indeed, published data indicate that infection with either the bacterium *Helicobacter pylori* or hepatitis A virus reduces the likelihood of developing asthma. Chang and colleagues have now provided more evidence in mice to support the idea that exposure of young children to infectious microorganisms can protect them from later development of asthma and identified an underlying mechanism to explain this protection (57–69). Infection of suckling mice with an influenza A virus protected the mice as adults from allergen-induced airway hyperreactivity (AHR), a hallmark of asthma. Protection was associated with the expansion of a subset of immune cells known as NKT cells, specifically, those NKT cells lacking expression of either CD4 or CD8. Further, upon transplantation into allergen-sensitized adult mice, these cells provided protection from subsequent allergen-induced AHR. Importantly, NKT cell–mediated protection from allergen-induced AHR could also be induced by treating suckling mice with a glycolipid derived from *H. pylori*. The authors therefore suggest that treating children with therapeutics that activate the $CD4^{-}CD8^{-}$ NKT cell population might prevent the development of asthma.

Mutations underlying rare human kidney disorder identified

Dicarboxylic aminoaciduria is a rare inherited disorder for which the affected gene has not yet been identified. Individuals with this disorder excrete extremely high levels of glutamate and aspartate in their urine, due to defective renal reabsorption. Half of the few patients reported thus far also exhibit mental retardation. Bailey and colleagues have now identified two loss-of-function mutations in solute carrier family 1, member 1 (SLC1A1) as causative for dicarboxylic aminoaciduria (446–453). The affected patients were homozygous for either of the two mutations (I395del and R445W). Functional analysis of the mutant proteins was performed in *Xenopus laevis* oocytes and indicated that they were severely or completely impaired in their ability to transport glutamate and cysteine. These data indicate the crucial role of SLC1A1 in renal glutamate and aspartate handling in humans. Furthermore, as SLC1A1 is the predominant neuronal glutamate transporter in the brain, the authors suggest that dicarboxylic aminoaciduria may predispose to neurological sequelae, including obsessive-compulsive disorder (OCD), consequent to the loss-of-function of SLC1A1.

Insight into how to design safer glucocorticoids



Glucocorticoids (GCs) and their synthetic analogs are used widely to treat transplant recipients and patients with numerous other conditions, including rheumatoid arthritis, asthma, and some forms of cancer. The beneficial effects of these drugs (e.g., dexamethasone) are a result of their potent antiinflammatory and immunosuppressive properties. However, their long-term use is limited by severe side effects, including hyperglycemia, hepatic steatosis (fatty liver), and type 2 diabetes. Several lines of previously published data led Patel and colleagues to hypothesize that the metabolic effects of GC drugs require the presence of nuclear receptors known as liver x receptors (LXRs) (431–441). Using mice lacking either LXRα or LXRβ or lacking both LXRs, it was shown that LXRβ is required to mediate many of the negative side effects of GC drugs. Specifically, LXRβ was required for dexamethasone-induced hyperglycemia, hyperinsulinemia, and hepatic steatosis. Importantly, it was not required for the immunosuppressive effects of dexamethasone. The authors therefore suggest that GC drugs designed to selectively activate the GC receptor and to not elicit involvement of LXRβ should cause fewer severe metabolic side effects than those currently in clinical use.